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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/011,797	07/23/98	PARMENTIER M	VANMA72.001A

HM22/0329

KNOBBE MARTENS OLSON & BEAR
620 NEWPORT CENTER DRIVE
SIXTEENTH FLOOR
NEWPORT BEACH CA 92660

EXAMINER	
MURPHY, J	

ART UNIT	PAPER NUMBER
1644	8

DATE MAILED: 03/29/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application N .	Applicant(s)	
	09/011,797	PARMENTIER ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1644	

-- The MAILING DATE of this communicati n appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *01 February 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-42,47-52,57 and 58* is/are pending in the application.

4a) Of the above claim(s) *48-52,57 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-42 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☒ Other: *Sequence Comparison A* .

DETAILED ACTION

Claims 1-34 were originally filed.

Claims 1-34 were canceled and new claims 35-58 were added in Paper No. 5, 7/23/98.

Claims 43-46 and 53-56 were canceled, and claims 39, 41-42, 48 and 57-58 were amended in Paper No. 7, 2/14/00.

Applicant's election of Group I, claims 35-42 and 47 in Paper No. 7, 2/14/2000 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 48-52 and 57-58 are withdrawn from further consideration by the examiner, 37 CFR 1.48(b).

Claims 35-42 and 47 are under consideration.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on an application filed in Belgium on 15/08/1995. Applicant has not complied with the requirements of 37 CFR 1.63(c), since the oath or declaration does not acknowledge the filing of any foreign application. A new oath or declaration is required in the body of which the present application should be identified by application number and filing date.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 40 is rejected under 35 U.S.C 112, first paragraph, because the specification, while being enabling for a polypeptide ligand of ORL1 selected from the group consisting of sequences set forth in SEQ ID Nos: 1, 2, 3 and 4, does not reasonably provide enablement for any other polypeptide ligand of ORL1. There is not adequate guidance as to the nature of the variants or derivatives which Applicants claim, i.e. differing polypeptide sequences which exhibit a similar activity to a specific polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with this claim.

Claim 40 is overly broad in the recitation of "ORL1 ligand", since no guidance as to what constitutes " ORL1 ligand" polypeptide is provided within the claims. The broad scope of claim 40 can be read to encompass any isolated polypeptide. There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a polypeptide other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the

disclosure. Given the breadth of claim 40 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim 38 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a substantially purified polypeptide comprising an amino acid selected from the group consisting of SEQ ID NOs:2, 3 and 4, does not reasonably provide enablement for an isolated peptide encoded by a polynucleotide which corresponds to at least 70% of the SEQ ID NO: 1 or its complementary strand. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 38-42 is overly broad in the recitation of "encoded by an isolated polynucleotide according to Claim 35" since no guidance is provided as to which of the myriad of polypeptide species encompassed by the claim will retain the characteristics of an ORL1 agonist. In the specification (page 3, lines 19-26), Applicants disclose that an agonist may be a molecule which mimics the peptide interaction with its receptor. Such may be analogs or fragments of the peptide according to the invention, or antibodies directed against the ligands binding side epitopes of the peptide receptors, or anti-idiotypic antibodies directed against particular antibodies which bind to receptor-interacting specific portions of the peptide according to the invention without disclosing any actual or prophetic examples on expected performance parameters of any of the possible muteins of ORL1 agonist. However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically

affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding an ORL1 agonist other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claim 38 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. Claims 39-42 are rejected insofar as they depend on the recitation of "encoded by an isolated polynucleotide according to Claim 35".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35-37, 40 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 40 is indefinite in that they only describe the peptide of interest by an arbitrary protein name. There is nothing in the claims which distinctly claims the protein and variants thereof. For example, others in the field may isolate the same protein and give said protein an entirely different name. Applicant should particularly point out and distinctly claim the peptide 3 molecule and variants thereof by claiming structural characteristics associated with the protein (e.g. amino acid sequence, molecular weight, etc.). Claiming biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly claim what that protein is.

Claim 37 is vague and indefinite in recitation of the phrase "a portion thereof having more than 15 nucleotides". It is suggested to change the phrase to " a portion thereof having more than 15 contiguous nucleotides".

Claim 37 is vague and indefinite in the recitation of the term "reconstitute". It is presumed that Applicant is claiming a polynucleotide that can hybridize and serve as a primer for PCR amplification. The claim language should be amended to reflect this.

Claims 35 and 36 are vague and indefinite in the recitation of "corresponds to". The metes and bounds of the claim would be more clearly delimited by the use of "% identical to". Claim 47 is rejected due to its dependence on the recitation in claim 35 of "corresponds to".

Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 9202554.

WO 9202554 discloses a polynucleotide with more than 15 nucleotides identical to the sequence set forth in SEQ ID NO: 1 (see Sequence Comparison A, attached), thus meeting the limitations of claim 37.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703-308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1644
March 16, 2000

Prema Mertz
PREMA MERTZ
PRIMARY EXAMINER

Sequence Comparison A

```
RESULT   1
US-08-514-451-5
; Sequence 5, Application US/08514451
;  GENERAL INFORMATION:
;    APPLICANT:  Bunzow, James R
;    APPLICANT:  Grandy, David K
;    APPLICANT:  Civelli, Olivier
;    APPLICANT:  Reinscheid, Rainer K
;    APPLICANT:  Nothacker, Hans-Peter
;    APPLICANT:  Monsma, Frederick J
;    TITLE OF INVENTION:  A Novel Mammalian Methadone-Specific
;    TITLE OF INVENTION:  Opioid Receptor Gene and Uses
;    NUMBER OF SEQUENCES:  6
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Banner & Allegretti, Ltd.
;      STREET:  10 South Wacker Drive, Suite 3000
;      CITY:  Chicago
;      STATE:  Illinois
;      COUNTRY:  USA
;      ZIP:  60606
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/514,451
;      FILING DATE:  11-AUG-1995
;      CLASSIFICATION:  530
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Noonan, Kevin E
;      REGISTRATION NUMBER:  35,303
;      REFERENCE/DOCKET NUMBER:  93,311-A
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  312-715-1000
;      TELEFAX:  312-715-1234
;      TELEX:  910-221-5317
;  INFORMATION FOR SEQ ID NO:  5:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  17 amino acids
;      TYPE:  amino acid
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-08-514-451-5


  Query Match             100.0%;  Score 86;  DB 9;  Length 17;
  Best Local Similarity   100.0%;  Pred. No. 7.5e-07;
  Matches   17;  Conservative    0;  Mismatches    0;  Indels    0;
Gaps    0;

Qy       1 FGGFTGARKSARKLANQ 17
           |||||||||||||||||
Db       1 FGGFTGARKSARKLANQ 17
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